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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,060	05/01/2001	Martin S. Linsell	P-090-R	4580
27038	7590	10/02/2003	EXAMINER	
THERAVANCE, INC. 901 GATEWAY BOULEVARD SOUTH SAN FRANCISCO, CA 94080			DESAI, ANAND U	
			ART UNIT	PAPER NUMBER

1653

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/847,060	<b>Applicant(s)</b> LINSELL, MARTIN S.	
	<b>Examiner</b> Anand U Desai	<b>Art Unit</b> 1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 26 September 2003.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 1-29 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \*   c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1</u>	6) <input type="checkbox"/> Other: _____

## **DETAILED ACTION**

### ***Specification***

1. The disclosure is objected to because of the following informalities: There is a typographical error on page 33, line 26. The word “allyl” appears to be intended to read “alkyl”.  
Appropriate correction is required.

### ***Claim Objections***

2. Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The method of claim 1 is to alkylating a glycopeptide, while the method of claim 15 is to isolating a glycopeptide.
3. Claims 6, 7, and 16 are objected to because of the following informalities: In claims 6, N,N-dimethylformamide is not presented with an abbreviation (DMF) so in claim 7 DMF is undefined. Insert (DMF) in claim 6 or spell out N,N-dimethylformamide in claim 7 in place of DMF. In claim 16, there is a typographical error on line 6, the characters “R<sup>3</sup> is” is duplicated.  
Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 3, 4, 6, 7, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The term "about" in claims 3, 4, and 9 is a relative term which renders the claim indefinite. The term "amount of reductive alkylation at the saccharide amine" is not defined by the claims 3, and 4 and "temperature range" is not defined by claim 9, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

7. Claims 6, and 7 recites a list of solvents, the use of "or" before dioxane in claim 6, and before methanol in claim 7, confuses what is an appropriate solvent. Is it all the chemicals before dioxane or dioxane that could be the solvent or is it each individual chemical independently selected which includes as a possible member, dioxane? If "or" is removed before dioxane the confusion would be removed.

8. Claim 11 recites the limitation "the acid" in claim 11, page 45, line 11. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 1, and 16 recites the term "suitable base", what is an unsuitable base compared to a suitable base? Not clearly defined.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Berglund et al. U.S. Patent 5,998,581 (Effective filing date=Nov. 21, 1996).

Berglund et al. teaches a method of reductive alkylating a saccharide amine containing glycopeptide. Claim 1 describes steps to prepare an N<sup>4</sup> (disaccharide-amine) alkylated glycopeptide antibiotic. The steps include reacting the glycopeptide with a ketone or aldehyde in the presence of a reducing agent selected from the group consisting of sodium cyanoborohydride and pyridine/borane complex (claim 1, 11, column 17-18; **Claims 1, 2, 8, 13, 14, 16-26**). The antibiotic is prepared in methanol (claim 2, column 18; **Claims 1, 2, 5, 6, 7, 8**). The pH is set within the acidic region between 6.3 and 7.0 (claim 8, column 18; **Claims 1, 11, 12**). The temperature can be carried out at 45°C (column 11, lines 19-20; **Claims 1, 9**). Berglund et al. teaches how the alkylated glycopeptide can be isolated by conventional techniques known in the art (column 11, line 49-50; **Claim 15**). In example 4, 2.5 g of A82846B (glycopeptide) was stirred in 250ml methanol (alcohol) and cupric acetate monohydrate (acid) was added. After stirring at ambient temperature for 10 minutes, 4'-chloro-4-biphenylcarboxaldehyde (aldehyde) and sodium cyanoborohydride (reducing agent) were added. Sodium hydroxide (base) was added at ambient temperature. Isopropyl alcohol was added to precipitate the alkylated glycopeptide. HPLC analysis of a reaction aliquot afforded a yield of 4.52 g (85.4%) of N4-(4-(4-chlorophenyl)benzyl)A82846B (alkylated at saccharide amine) (Columns 12, line 65 through Column 13, line 22; **Claims 1-26**).

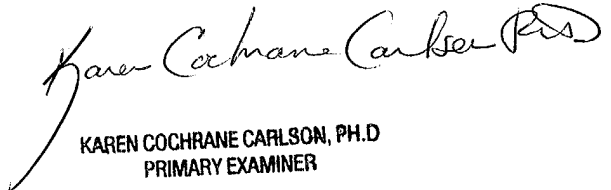
***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claims 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berglund et al. U.S. Patent 5,998,581 (Effective filing date=Nov. 21, 1996) in view of Ramakrishnan et al. U.S. Patent 4,698,327. Berglund teaches a method of alkylating a glycopeptide antibiotic and Ramakrishnan teaches pharmaceutical formulations of glycopeptide antibiotics. Therefore, it would have been obvious to a person having ordinary skill in the art to prepare a pharmaceutically acceptable salt of the alkylated glycopeptide. Further, combining a pharmaceutically acceptable carrier with the salt to provide a pharmaceutical composition **(Claims 27-29)**.

September 26, 2003



KAREN COCHRANE CARLSON, PH.D  
PRIMARY EXAMINER